

Case Reports

Neonatal Cardiac Allotransplantation Facilitated by In Utero Diagnosis of Hypoplastic Left-Sided Heart Syndrome

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WITH RECENT IMPROVEMENTS in fetal echocardiography, an accurate diagnosis of congenital heart disease before birth is now feasible. Several reports dating from 1983 conclude that with prenatal diagnosis, rapid and specific postnatal intervention may improve survival.¹⁻⁸ We report a case of a neonate with the hypoplastic left-sided heart syndrome diagnosed in utero who received a cardiac allograft at 3 hours of age after cesarean delivery at 37 weeks' gestation. We believe this is the youngest transplant recipient reported to date in the literature.

Report of a Case

In Utero Diagnosis

A 35-year-old woman, gravida 3 para 1, underwent fetal echocardiography at 18 weeks' gestation because of a family history of cardiac disease. A second study at 24 weeks' gestation showed cardiac asymmetry with the following findings: an enlarged and hypertrophied right ventricle, an atretic mitral valve, and a severely hypoplastic left ventricle leading to a small and hypoplastic ascending aorta and aortic arch. The hypoplastic left-sided heart syndrome was confirmed by a third fetal echocardiogram at 27 weeks' gestation. An amniocentesis at 29 weeks revealed a normal 46 XY karyotype. Fetal blood sampling to determine blood type was not done at this time as treatment options had not been delineated. The diagnosis was explained to the family and a referral made to Loma Linda University Medical Center (LLUMC).

Preoperative Evaluation

The parents consulted with the multidisciplinary heart transplant team. Fetal echocardiography at LLUMC during the 35th week of gestation confirmed the diagnosis of a hypoplastic left-sided heart syndrome (Figure 1). The following options were outlined: no intervention, a palliative Norwood procedure,⁹ or cardiac transplantation.^{10,11} After extensive discussion and consideration, the parents chose to attempt heart transplantation.

The mother had previously undergone a uterine cornual

resection with a tubal pregnancy, hence was not a candidate for labor and vaginal delivery. Obstetric sonography showed findings consistent with 36 weeks' gestation with an estimated weight of 3.0 kg. The fetus was registered as a possible recipient for an "O" (universal) donor as his blood type was unknown.

A potential donor was identified soon after registration, and the recipient family was transported to LLUMC in preparation for delivery. The donor was a 2-day-old 2.7-kg anencephalic neonate who showed cessation of brain-stem function, including an absence of respiratory effort after appropriate carbon dioxide stimulation. The blood type was O, Rh positive.

Delivery and Heart Transplantation

With a donor heart waiting and the recipient fetus at 37 weeks' gestation, fetal pulmonary maturity studies of amniotic fluid were not done. A low-segment transverse cesarean section was done without complication using epidural anesthesia, and a 2.9-kg male neonate was delivered. One- and five-minute Apgar scores were 8 and 8, respectively. The umbilical cord blood arterial pH was 7.31, and the venous pH was 7.39.

The infant's condition deteriorated rapidly, with an arterial blood gas measurement showing a pH of 6.96 and a base deficit of -16 ten minutes after birth. Mechanical ventilation was begun with the concentration of inspired oxygen at 40%. Treatment with increased peak inspiratory and positive end-expiratory pressures improved the pH to 7.30, but the partial oxygen pressure remained at 16 torr. The findings of a chest roentgenogram were consistent with retained lung fluid.

Peripheral perfusion was poor. A striking left leg pallor developed, and there was intermittent mottling of the upper extremities. After umbilical venous and arterial lines were placed, infusions of prostaglandin E₁, cyclosporine, antibiotics, and steroids were started. The left leg pallor cleared with the prostaglandin infusion. Postnatal echocardiography confirmed a hypoplastic left-sided heart syndrome, with the foramen ovale marginally patent. The clinical picture was consistent with insufficient peripheral perfusion complicated by restrictive intra-atrial mixing.

Within three hours of birth, the newborn was taken to the operative department where orthotopic heart allotransplantation was done using general anesthesia, extracorporeal circulation, and profound hypothermic circulatory arrest. The donor heart recovery was accomplished in an adjacent surgery. The total cold ischemic time for the donor heart was 95 minutes. The baby left the operating room with stable hemodynamics, a good urine output, and a regular sinus rhythm.

Postoperative Course

The newborn's neurologic recovery was rapid. His respiratory recovery was complicated by increased pulmonary vascular resistance treated with 100% inspired oxygen. Inotropic support was provided using an infusion of dopamine hydrochloride, dobutamine hydrochloride, and isoproterenol hydrochloride. Peritoneal dialysis was required for the first four postoperative days because of impaired renal function. The endotracheal tube was removed on the seventh postoperative day. On the 35th postoperative day, the baby was dis-

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charged from the hospital on a regimen of cyclosporine and azathioprine.

He was treated briefly on three occasions with oral prednisone regimens for presumed rejection early in his postoperative course. He has received no corticosteroid therapy beyond 6 weeks of age. At the time of manuscript preparation, 22 months after the transplant, the infant appears to be developing and growing normally.

Discussion

Since November 1985, 46 babies (younger than 6 months) with the hypoplastic left-sided heart syndrome or other uncorrectable heart disease have undergone cardiac allotransplantation at LLUMC. Of these infants, 41 are surviving with essentially normal growth and development at 1 to 44 months after the transplant. Reasonable results have also been obtained with staged surgical palliation (the Norwood operation). The encouraging outcome of these surgical options challenges the more traditional approach of "letting nature take its course," with the death of these babies being the inevitable end point.

In Utero Diagnosis

The primary issue raised by this case focuses on the potential advantages and disadvantages of the in utero diagnosis of a hypoplastic left-sided heart syndrome and other severe or lethal congenital heart disease (Table 1).

Prenatal counseling. When the diagnosis is made postnatally with the stress of a deteriorating newborn baby overwhelming the parents, a discussion of management options is less than optimal. The pressure of having to make a major decision at a time of high anxiety can lead to parental misunderstanding and frustration. While a prenatal diagnosis may prolong the duration of uncertainty, decisions regarding postnatal management can take place in an environment of organization and thoroughness.

Time for family relocation. An early diagnosis affords time for relocation and reorganization of family life if the option of heart transplantation is chosen. To facilitate follow-up care during the time when rejection of the new heart is most likely, the family must plan to live in close proximity to the transplant center for as long as six months after the transplant. In utero diagnosis allows time to make

TABLE 1.—Possible Advantages and Disadvantages of In Utero Diagnosis

Advantages

- Prenatal counseling regarding management options
- Time for relocating family
- Additional time for donor search
- Allows time for planned delivery in well-equipped facility
- Eliminates delay in definitive diagnosis and treatment

Disadvantages

- Risk of misdiagnosis
- Prolonged emotional distress
- Prematurity may lead to a difficult early postoperative course

this transition before the concerns of newborn transplant surgery are placed on the family.

Time for a donor search. If a diagnosis is made in utero, additional time is gained for finding a suitable donor. Heart transplantation as a therapeutic option is currently limited by the paucity of donor organs. Since November 1985 at LLUMC, about 30% of infants registered for transplantation have died awaiting a replacement organ. Prenatal diagnosis allows the search for a donor heart to be carried out while the recipient fetus remains stable in utero. During this time a fetal chromosomal evaluation can be done to rule out major karyotypic abnormalities. Donor-recipient matching requires a knowledge of blood type and weight limits. Although not carried out in our case, Vincent and co-workers suggest fetal blood sampling for donor matching purposes.¹²

Timed delivery. When an appropriate donor is found, the mother can be transported to the transplant center where a planned delivery of the recipient fetus can take place. If the recipient fetus is at or near term, labor can be induced if the condition of the mother's cervix is favorable. Babies with the hypoplastic left-sided heart syndrome generally have no difficulty coping with the stress of labor. If labor is contraindicated or the cervical condition is unfavorable, a cesarean delivery may be appropriate as in our case. Careful clinical judgment must be exercised if a donor becomes available before the recipient fetus achieves pulmonary maturity. The risks of not using an available donor heart must be balanced with the potential of postoperative respiratory distress due to pulmonary immaturity.

Diagnosis and treatment expedited. An accurate in utero diagnosis can eliminate the frequent delay in definitive diagnosis of congenital heart disease when various other pathologic disorders, such as pulmonary hypertension, sepsis, and severe pneumonia, are being ruled out. Huhta and associates described a case of in utero diagnosis of critical aortic stenosis.¹³ The neonate underwent a successful emergency aortic valvotomy at 12 hours of age. In the case of the Loma Linda baby, the rapidity of his deterioration after birth probably would have resulted in his death had not the diagnosis been made antenatally and his mother transferred to the transplant center. Conversely, an incorrect or hasty prenatal diagnosis rendered by inexperienced fetal echocardiographers can lead to unnecessary transport of mothers to transplant centers and needlessly compound parental anxiety.

Anencephalic Donors

Babies born with anencephaly have been considered as possible solid organ donors because of the absence of the cerebral cortex, the lethal nature of the defect, and because

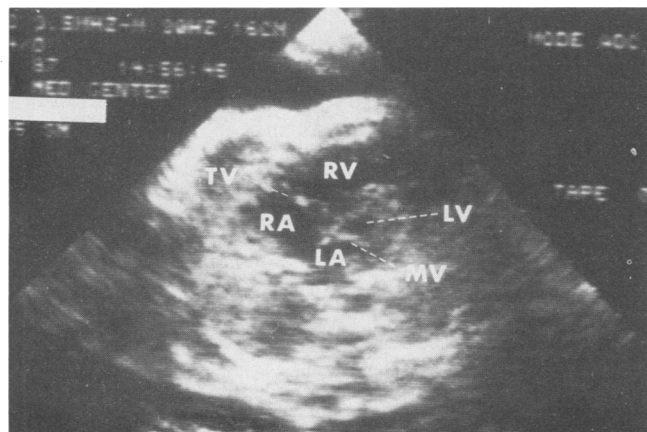


Figure 1.—A fetal echocardiogram with a 4-chamber view of the heart at a gestational age of 35 weeks shows a hypoplastic left ventricle (LV) with mitral atresia and an enlarged right ventricle (RV). LA = left atrium, MV = mitral valve, RA = right atrium, TV = tricuspid valve

other visceral organs are usually structurally normal. An anencephalic newborn provided the donor heart in our case.

Brain death in the anencephalic baby was determined using criteria described by Ashwal and Schneider¹⁴⁻¹⁶: coma, an absence of sustained spontaneous respiration when the arterial carbon dioxide pressure is greater than 60 torr, pupils fixed and dilated, an absent oculocephalic reflex (doll's eyes), absent gag and corneal reflexes, normothermia, no use of narcotics, and the blood barbiturate concentration is below therapeutic values.

The successful use of an anencephalic neonate's organ has led to both hopes and concerns about these babies as possible donor sources.¹⁷⁻²⁰ National attention has been captured as the profound moral, ethical, and legal dimensions of this controversial issue have been reexamined from opposing perspectives.

Prompted by parental request, Loma Linda University Medical Center implemented a protocol devised to study the possibility of organ procurement from anencephalic newborns.²¹ The study protocol called for placing an anencephalic newborn on a respirator for a maximum of a week while observing for the occurrence of brain death. Although 12 infants were evaluated over a period of nine months, no successful solid organ donations were realized, and the protocol was abandoned.²²

Conclusion

Our experience with in utero diagnosis of the hypoplastic left-sided heart syndrome and subsequent transplantation is limited to this single case, the significance of which remains to be established in a larger series. This case shows, however, that it is possible for the in utero diagnosis of the syndrome to improve the chances of locating an appropriate donor. Furthermore, it is possible to successfully transplant a heart into a newborn a few hours after birth.

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Carcinoid Tumors of the Thymus

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WHEN ROSAI AND HIGA first described carcinoid tumors of the thymus, they differentiated them from the more commonly occurring thymomas¹ and defined their association with Cushing's syndrome and multiple endocrine neoplasia.^{1,2} We report the cases of six patients with carcinoid tumors of the thymus treated at The University of Texas MD Anderson Cancer Center (Houston) between 1950 and 1988, including their natural history, clinical presentation, endocrine manifestations, and response to therapy.

Report of Cases

Case 1

The patient, a 20-year-old man, was referred to MD Anderson Cancer Center for evaluation of recurrent Cushing's syndrome two years after he began having central obesity and proximal muscle weakness. A computed tomographic (CT) scan revealed a mass in the anterior mediastinum and enlarged adrenal glands. Partial resection had been undertaken, and pathologic examination had revealed carcinoid tumor of the thymus. Postoperative radiotherapy followed. Symptoms and signs of Cushing's syndrome recurred two years later, and the patient underwent reexploration and partial excision of the carcinoid tumor. Postoperatively, the use of metyrapone controlled the symptoms only partially.

When he was referred to us for evaluation, he had cushingoid signs and symptoms. Laboratory evaluation elicited the following values: an elevated cortisol level of 1.08 μmol per liter (normal, 0.22 to 0.67); adrenocorticotrophic hormone (ACTH), 283 and 256 ng per liter (normal, 0 to 70); urinary 17-hydroxysteroids, 436.6 μmol per day (normal, 5 to 25); urinary 17-ketosteroids, 170.27 μmol per day (normal, 20 to 70); and urinary 5-hydroxyindoleacetic acid (5-HIAA), 31.5 μmol per day (normal, 10 to 45). A skeletal survey and bone scan revealed metastases in the sixth thoracic vertebra, both femurs, the pelvis, and the right humerus.

Bilateral adrenalectomy resulted in remission of the Cushing's syndrome, and postoperative chemotherapy consisting of fluorouracil, doxorubicin hydrochloride, and strep-

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